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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/428,458	10/28/1999	KJETIL TASKEN	Q-56244	4681

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EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/428,458	TASKEN ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40,45,48 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *40* is/are allowed.

6)☒ Claim(s) *45, 48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 12/27/2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 6/29/2005 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 40, 45, 48 and 49 are pending in the application.

Response to Arguments--35 USC § 103

Claims 45, 48 and 49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gjertsen, in view of Hofmann et al. and Jastorff et al. (WO 93/21929), for the reasons of record set forth in the office action mailed 6/29/2005.

Applicant asserts that cAMP is a signaling molecule that has many functions in cells and is responsible for controlling many pathways and many biological processes in all cell types. Applicant asserts that therefore the effect demonstrated in Hoffman et al. could be attributed to any of many pathways or indeed it could be a non-specific effect. Applicant asserts that the Hofmann et al. merely states that cAMP may be involved in T cell proliferation. Hofmann et al. teach that restoration of normal T cell functions should be of great benefit in the treatment of HIV infection and further that T cell function was

restored by reducing intracellular cAMP levels with adenosine analogues. Applicant argues that Hofmann et al. does not indicate how to apply this teaching to the treatment of diseases. In response to applicant's argument, it is noted that the features upon which applicant relies (i.e., a teaching to the treatment of diseases) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This argument is considered irrelevant since the instant claims do not recite a treatment effect.

Applicant further argues that there is no specific teaching in Hofmann et al. whatsoever to use specific inhibitors of the PKA Iα pathway as claimed in the present invention. It is noted that the features upon which applicant relies (i.e., a teaching regarding specific inhibitors of the PKA Iα pathway) are not recited in the rejected claim(s). This argument is considered irrelevant since the instant claims do not recite activity in the PKA Iα pathway. However, even if the instant claims did recite such a limitation, the cAMP antagonist taught by Hofmann et al. to restore T cell function would inherently act through the pathway influencing T cell proliferation. As stated in applicant's own argument, cAMP has a wide range of effects and acts in all cells. Any drug, including the cAMP antagonist taught by Hofmann et al., would operate globally. Additionally, Hofmann et al. was not relied upon for the teaching of the instantly recited compound, but was relied upon for the teaching regarding restoration of T cell function in HIV infection by reduction of intracellular cAMP levels with adenosine analogues.

The examiner relied on Gjertsen et al. and Jastorff et al. for the teaching of specific cAMP antagonists.

Applicant argues that administering such broad spectrum inhibitors as taught by Hofmann et al. would be undesirable owing to the large number of undesirable side effects which are likely to result and further that Hofmann et al. do not illustrate whether effecting all cAMP pathways would be beneficial *in vivo*. As explained above, the examiner did not rely upon Hofmann et al. for such teachings, but relied on Hofmann et al. strictly for the teaching regarding restoration of T cell function in HIV infection by reduction of intracellular cAMP levels with adenosine analogues. Contrary to applicant's various arguments regarding Hofmann et al., the instant claims only require a teaching of a method for enhancing T cell proliferation in a subject in need thereof and do not require any teaching regarding treatment effects or action in a specific cAMP pathway.

Applicant argues that although certain PKA type Iα inhibitors were known at the date of the invention, there is nothing in the cited documents that would indicate that they could be used to treat a subject in need of enhanced T cell proliferation. Contrary to applicant's argument, one would have reasonably expected the instantly recited cAMP antagonists could be used to treat a subject in need of enhanced T cell proliferation because Gjertsen et al. and Jastorff et al. teach the instantly recited compounds and Hofmann et al. teach restoration of T cell function in HIV infection by reduction of intracellular cAMP levels with adenosine analogues. As stated by the applicant in the instant argument, cAMP is involved in a multitude of pathways and cell

types. With the teaching that cAMP antagonists could be used to restore T cell function in HIV infection by Hofmann et al., one would be motivated to utilize the antagonists taught by Gjertsen et al. and Jastorff et al. in the same manner because the compounds were known to be cAMP antagonists and had been utilized *in vivo* by Jastorff et al.

Applicant argues that Jastorff et al. indicate that the effects of cAMP on cell proliferation are contradictory and refers to contradictory results obtained on the proliferation of lymphocytes on page 3. Applicant asserts that this is a clear teaching against using such compounds in the context of enhancing proliferation of T cells. Contrary to applicant's argument, Jastorff et al. teach that a role for cAMP in cell differentiation seems to be established but that it is much more difficult to define a general function for this nucleotide in the regulation of cell proliferation. Jastorff et al. teach that the data are interpreted differently. Contrary to applicant's assertion, this is not a teaching against using such compounds in the context of enhancing proliferation of T cells, but rather indicates that the research is not yet conclusive. Rather than teaching away, Jastorff et al. do not provide T cell experiments and therefore are silent as to the effect on T cell proliferation. The teachings of Jastorff et al. relied upon by the applicant support that cAMP has a role in different cell types.

Further, Jastorff et al. was primarily relied upon by the examiner to establish that the instantly recited compounds were known in the art at the time the invention was made and had been administered *in vivo* to study tumor growth. Additionally, Jastorff et al. are relied upon for establishing that the Rp form is a better candidate for

chemotherapy since they are more resistant to hydrolysis. Jastorff et al. teach the instantly recited compounds which applicant argues are specific for PKA type Iα.

Applicant argues that the compounds taught by Jastorff et al. were shown to inhibit growth and would therefore not be contemplated for use in a method which is required to cause a positive effect on cell proliferation. It is acknowledged that the compounds taught by Jastorff et al. demonstrated inhibition of growth of HL-60 leukemia cells. However, Jastorff et al., as well as the instant applicant, each teach that cAMP is present in all cells and a multitude of pathways. Jastorff et al. are silent as to the effect of such compounds in T cell proliferation. The inhibitory effect in HL-60 leukemia cells is not correlative to the effect of such compounds with regards to T cell proliferation, as supported by applicant's assertions that there are variable effects on different cell types.

Since Hofmann et al. teach the restoration of T cell function in HIV infection by reduction of intracellular cAMP levels with adenosine analogues, one would be motivated to utilize the compound taught by Jastorff et al. to determine the effect on T cell function, particularly since Jastorff et al. teach that the Rp form is a better candidate for chemotherapy since they are more resistant to hydrolysis.

Applicant argues that Jastorff et al. fails to show that enhanced T cell proliferation would be achieved and therefore cannot illustrate a reasonable expectation of success. On the contrary, Jastorff et al. was not relied upon for a teaching of enhanced T cell proliferation. As explained above, Jastorff et al. are silent as to such teachings. Hofmann et al. was relied upon for teaching enhanced T cell proliferation. It is the combination of the references that the examiner has relied upon to establish an

expectation of success. Specifically, Hofmann et al. teach the restoration of T cell function in HIV infection by reduction of intracellular cAMP levels with adenosine analogues. Gjertsen et al. teach a method of inhibiting cAMP with cAMP antagonists and specifically teach Rp-8-Br-cAMPs, RP-8-Cl-cAMPs and Rp-8-(4-chlorophenyl-thio)-cAMPs. Gjertsen et al. teach that inhibition of cAMP results in enhanced DNA replication. Jastorff et al. was also relied upon by the examiner to establish that the instantly recited compounds were known in the art at the time the invention was made and was further relied upon for teaching *in vivo* administration to study tumor growth. Additionally, Jastorff et al. is relied upon for establishing that the Rp form is a better candidate for chemotherapy since they are more resistant to hydrolysis. Since the instantly recited compounds were known in the art at the time the invention was made to inhibit cAMP and enhance DNA replication, it would have been obvious to one of ordinary skill in the art to utilize these compounds in the method taught by Hofmann et al. to restore T cell proliferation. Hofmann et al. specifically teaches T cell restoration via reducing intracellular cAMP levels. Gjertsen et al. and Jastorff et al. each teach the instantly recited compounds which were known to be cAMP antagonists. Therefore, one would reasonably expect for these compounds to function in the method taught by Hofmann et al.

Applicant argues that the experiments in the present application used purified preparations, whereas the prior art may have had contradictory effects due to impure compounds. In response to applicant's argument, it is noted that the features upon which applicant relies (i.e., purity of the compound) are not recited in the rejected

claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This argument is considered irrelevant since the instant claims do not recite a limitation regarding purity.

Applicant argues that Gjertsen et al. examine the effect of compounds on PKA, but that Gjertsen et al. does not perform any experimental work based on T cells. The examiner did not rely on Gjertsen et al. for a teaching regarding T cells, but rather relied on Gjertsen et al. for teaching inhibition of cAMP with cAMP antagonists (Rp-cAMPs analogs) in cell culture. Gjertsen et al. specifically teach Rp-8-Br-cAMPs, RP-8-Cl-cAMPs and Rp-8-(4-chlorophenyl-thio)-cAMPs. Gjertsen et al. teach that inhibition of cAMP results in enhanced DNA replication. Applicant states that if the skilled person had assessed proliferation of T cells with the compounds of Gjertsen et al., no proliferation would have been observed since proliferation is seen in cells from HIV infected patients but not in normal T cells. This argument is considered supportive of the combined teachings of Hofmann et al. with Gjertsen et al., as relied upon by the examiner. As stated above, the examiner has established a strong motivation to utilize the compounds taught by Gjertsen et al. in the method of Hofmann et al. The skilled artisan would in fact have observed T cell proliferation, as demonstrated by applicant's own argument. Applicant asserts that if the skilled person had chosen to assess the effect of the compounds on T cell proliferation, the results would have led the skilled person to believe that the compounds were ineffective at enhancing proliferation because the inhibitors do not affect normal T cells. On the contrary, the skilled artisan

would have been testing the compounds on T cells of HIV infected individuals due to the teachings of Hofmann et al. which were relied upon as a basis for this rejection.

Additionally, applicant's arguments that rely upon the difference between T cells of HIV infected patients and normal T cells are focused upon features that are not recited in the rejected claim(s). The instant claims do not recite any limitation wherein HIV is treated or cells of HIV infected individuals are targeted.

Applicant asserts that the use of hindsight is required to selectively interpret and combine the prior art documents. Contrary to applicant's assertion, Hofmann et al. explicitly teaches that T cell function is restored in HIV infection by reduction of intracellular cAMP levels with adenosine analogues. Since the instantly recited compounds were known to be cAMP antagonists and cAMP was known to be present in all cells and function in a multitude of pathways, there is no apparent reason why one of ordinary skill in the art would not have utilized the instantly recited compounds to achieve the result taught by Hofmann et al.

Therefore, the 35 U.S.C. 103(a) rejection set forth in the official office action mailed on 6/29/05 is considered proper and maintained.

Allowable Subject Matter

Claim 40 is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Amy H. Bowman
Examiner
Art Unit 1635

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER